

Familial hypertrophic cardiomyopathy in Ceylon

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Forty patients had a diagnosis of hypertrophic cardiomyopathy confirmed by right and left heart catheterization or necropsy. The families of the patients were investigated and 15 of the 40 had a positive family history. In these 15 families, 79 parents and sibs were alive, and 55 were found to have evidence of the disease. Of the 55, 40 were male and 15 female. The familial incidence was 37.5 per cent. The sex ratio in the familial cases was male-to-female 2.7:1 and in the sporadic cases 2.2:1.

Since the description by Brock (1957) and Teare (1958), a large number of papers has appeared on the condition named hypertrophic obstructive cardiomyopathy in the United Kingdom and idiopathic hypertrophic subaortic stenosis in the United States. As inflow or outflow obstruction of the left ventricle is not an essential feature we prefer the term hypertrophic cardiomyopathy suggested by Goodwin (1970).

At the 1970 Ciba Symposium on this subject Nellen (1971) from South Africa and Braunwald from the U.S.A. mentioned that most of the cases appeared to be among the Caucasian races and that the incidence among Africans and American Negroes was quite low (Wolstenholme and O'Connor, 1971). The disease appears to be not uncommon in Ceylon. In this paper we present 55 cases of hypertrophic cardiomyopathy occurring among 101 members of 15 Ceylonese families.

Subjects and methods

This study was started in 1968, when a brother and a sister, both in their teens, were referred to us suffering from angina of effort. They were members of a family of 9 sibs (Fig. 1, 2, and 3), one of whom had died suddenly in his late teens. The symptomatic male sib also died suddenly on mild exertion and a necropsy revealed a massive heart with a very thick septum and left ventricle (Fig. 4).

Since then we have diagnosed the condition in a further 38 patients by right and left heart catheterization

and angiocardiology (Fig. 5) and still another at a necropsy on a young man who fell dead while running for a bus (Fig. 6, 7, and 8), giving a total of 40 patients.

The immediate families, that is, parents, sibs, and children of these patients were studied clinically and by radiography, electrocardiography, and phonocardiography, a few also by cardiac catheterization. A positive family history was obtained in 15 of these 40 patients.

These 15 families had a total of 79 parents and sibs alive, while 22 of them had died. The maximum possible information about the latter was obtained.

Findings

The families were not interrelated. They were not confined to any particular area of Ceylon. The two major communities in the island the Sinhalese and Tamils were both involved. Of the 79 members of the 15 families, 55 were found to have evidence of the disease (53 on investigation and 2 at necropsy). Of these, 40 were male and 15 were female.

Of the 55 cases, 26 had symptoms and 29 were asymptomatic. The common symptoms complained of were dyspnoea on effort, angina on effort, palpitation, fatigue, and dizziness. The 29 asymptomatic patients had abnormal auscultatory, electrocardiographic, radiographic, and phonocardiographic findings. A very few with florid signs, x-ray, and electrocardiographic findings were completely asymptomatic.

The common signs in these patients were systolic murmur over the praecordium, cardiac enlargement, especially of the left ventricle, double apical beat, and a fourth heart sound.

Electrocardiographic findings were T wave and ST abnormalities, prolonged QRS complex, right bundle-branch block, and pathological Q waves. Only one patient had atrial fibrillation. Frank and Braunwald (1968) and Goodwin (1970) reported a

Received 16 June 1972.

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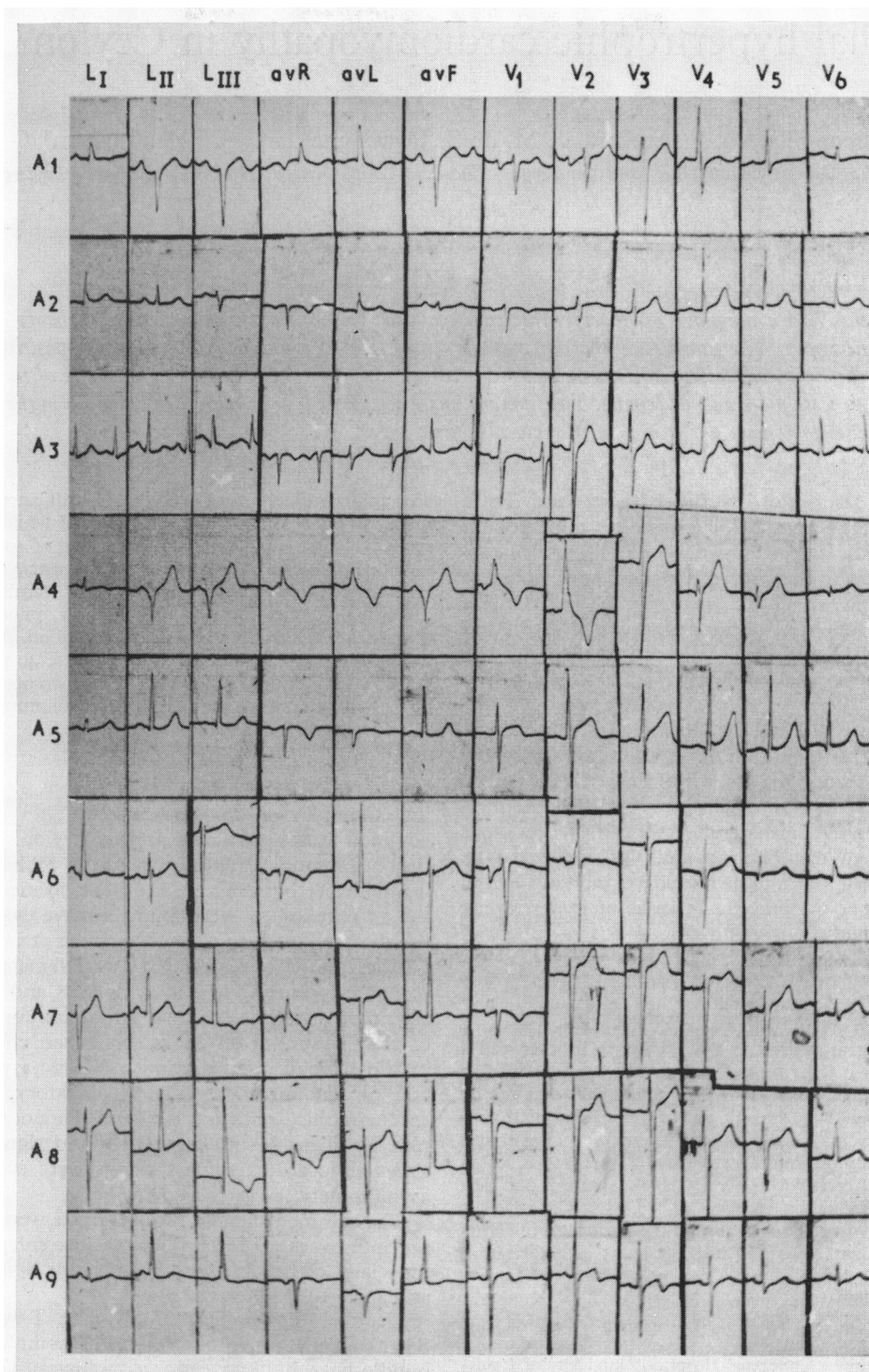


FIG. 1 *Electrocardiogram of parents and 7 live sibs of Family No. 1 (electrocardiograms of 2 dead sibs not available).*

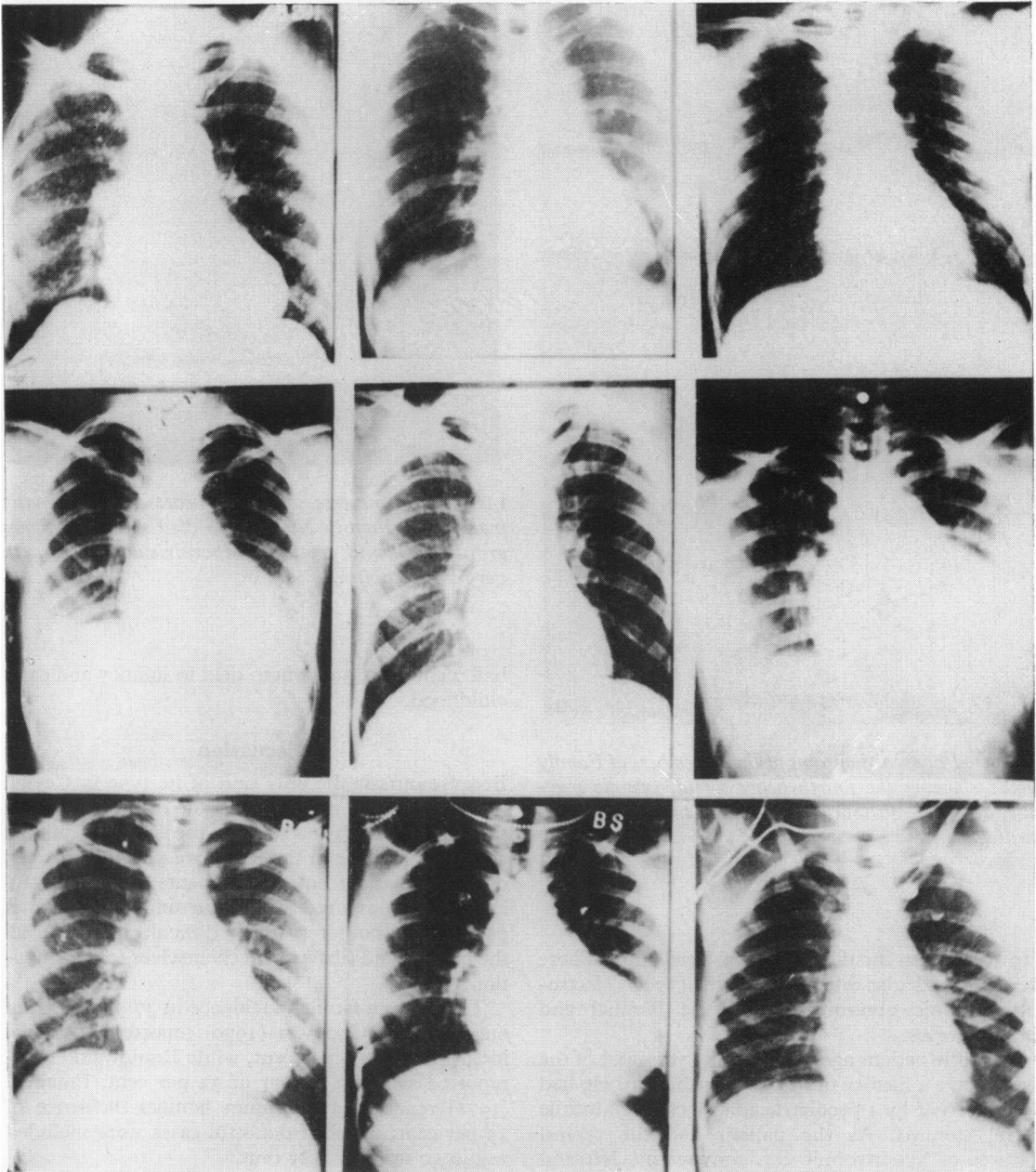


FIG. 2 Chest x-rays of parents and 7 living sibs of Family No. 1. — Left to right, horizontally, x-rays refer to patients whose electrocardiograms are marked (in Figure 1) A1, A2, A3 (top row); A4, A5, A6 (middle row); A7, A8, A9 (bottom row).

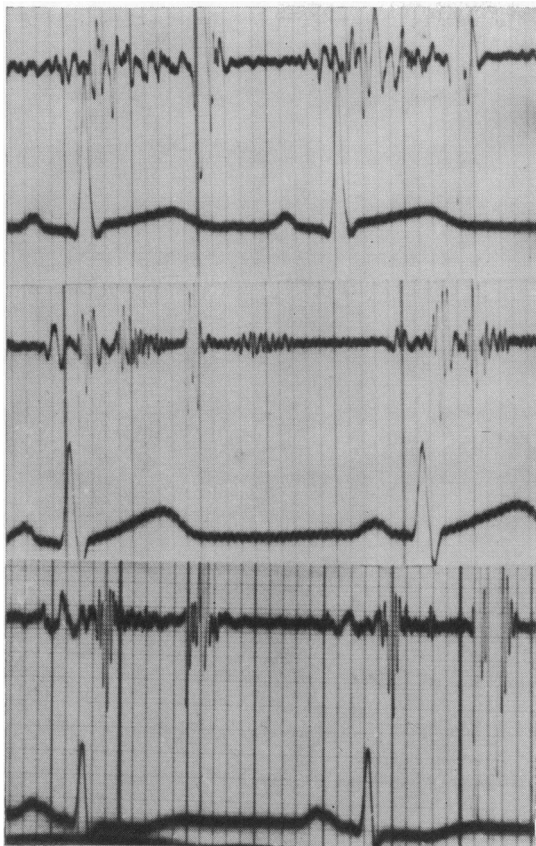


FIG. 3 Phonocardiograms of three members of Family No. 1 showing the fourth heart sound, systolic murmur, and mid-diastolic murmur in one (middle phonocardiogram).

5 to 10 per cent incidence of atrial fibrillation. There were no particular differences in the type of electrocardiographic abnormalities in the familial and sporadic cases.

Only one patient age 11 years, the youngest of the series, gave a history of systemic embolism. He had been referred by a paediatrician as a case of juvenile mitral stenosis. As the patient had the typical features of hypertrophic cardiomyopathy, left and right heart catheterizations were done confirming the diagnosis.

None of the patients gave a history of infective endocarditis or of heart failure.

Only one female sib had married and given birth to children. She was asymptomatic, but had abnormal electrocardiographic and x-ray findings. She

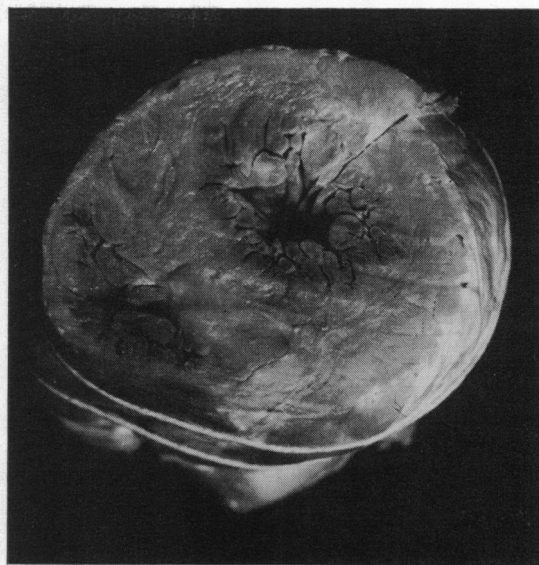


FIG. 4 Transverse section of heart of symptomatic male sib of Family No. 1, who died suddenly, shows grossly thickened septum and ventricular wall, with very small cavity.

had 7 children, 3 of whom died in infancy and early childhood.

Discussion

Because ours is the only unit of its type in Ceylon (population 12.5 million), and the distance between the extreme north and south of the island is less than 300 miles, we are in the fortunate position that not only is a great percentage of patients with a doubtful cardiac diagnosis referred to our unit, but also it is possible, without too much difficulty, to have all the parents and sibs present themselves for examination.

There was a familial incidence in 37.5 per cent of our patients; Goodwin (1970) reported a familial incidence of 14.5 per cent, while Braunwald (1971) reported a family history of 32 per cent. Emanuel (1971) reported a minimum familial incidence of 25 per cent, which if doubtful cases were included would go up to 37 per cent.

The sex ratio in our familial cases was 40 male to 15 female cases (2.7:1); in the sporadic cases the ratio was 17 male to 8 female (2.1:1); Braunwald *et al.* (1964) had a 1:1 ratio in the familial cases and 4:1 ratio in his sporadic cases. Emanuel (1971) reported a male-to-female ratio of 1.5 to 1 in familial and 1.7:1 in sporadic cases.

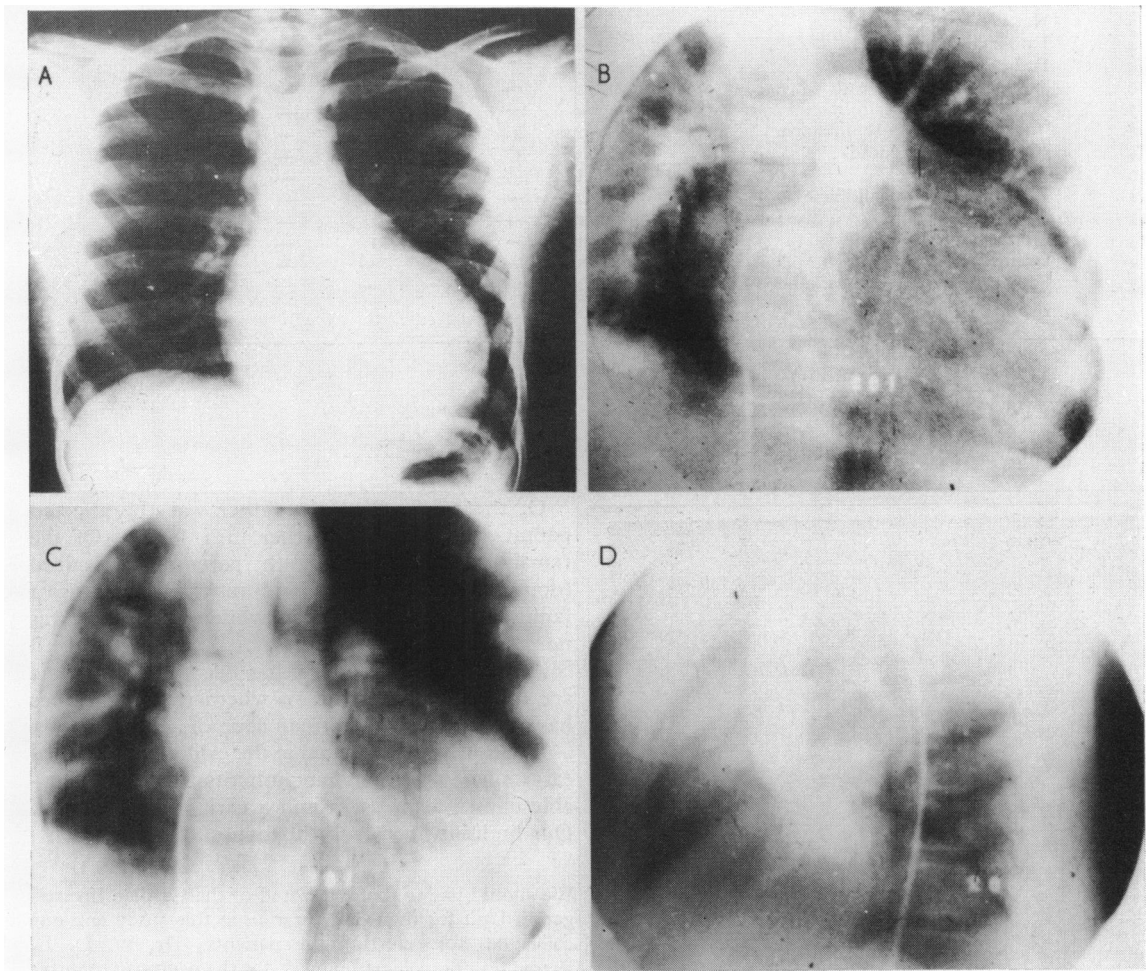


FIG. 5 *Composite picture of investigations of a sib of Family No. 5. (A) Teleradiogram; (B) right ventricular angiogram showing thick septum; (C) on follow-through hold-up of dye in left atrium is seen; (D) left ventricular angiogram showing mitral incompetence.*

TABLE Incidence among families

Family No.	Affected parent	Affected sibs living		Normal sibs living		Sibs dead		Total no. of children
		M	F	M	F	M	F	
1	Father	3	3	1	—	2	—	9
2	Father	5	1	—	—	—	—	6
3	Not known, both dead	4	2	—	—	—	—	6
4	Father	1	2	—	—	—	—	3
5	Father	2	1	2	1	—	—	6
6	? Mother (sudden death — history of palpitation)	1	—	2	—	—	—	3
7	Father	1	1	1	—	—	—	3
8	? Father dead, cause unknown	1	2	1	1	—	—	5
9	Not known, both dead	3	1	—	—	—	—	4
10	Father	1	—	3	2	—	—	6
11	? Mother died at childbirth	2	—	—	—	—	6	8
12	? Father dead, unknown cause	2	—	—	1	—	—	3
13	Mother	1	—	—	1	—	—	2
14	Father	3	—	1	—	—	—	4
15	Father dead, ? cause of mother's death ? Myocardial infarction	1	—	—	—	2	—	3

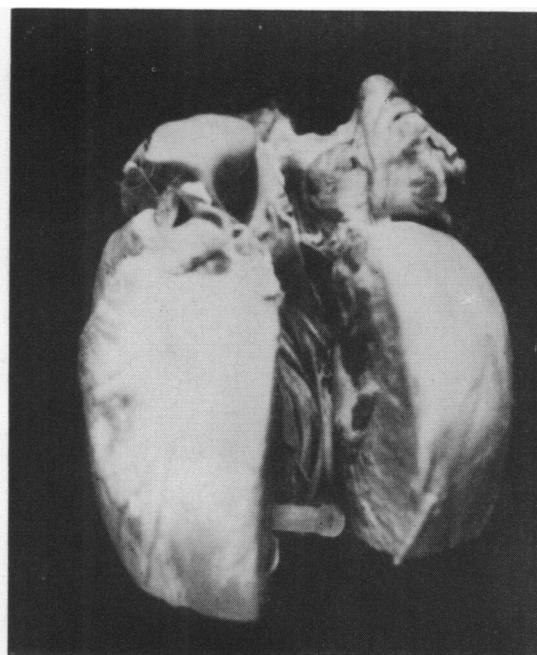


FIG. 6 Longitudinal section of heart of the second patient who died suddenly while running for a bus shows a very thick left ventricular wall and small cavity.

Of the 15 families, the father was the affected parent in 7 and the mother in 1 family. Of the remaining 7 families, both parents were dead (doubtful causes in 3), and in the remaining 4 families, 1 parent was dead while the 1 living was normal (Table).

As our follow-up period has been very short, we are unable to comment on whether familial cases have a worse prognosis than sporadic cases.

Emanuel (1971) states that the evidence in familial cases suggests a dominant inheritance with a variable clinical expression and a variable penetration. Our findings fit in with this hypothesis.

We should like to thank the staff of the Cardiac Investigation Unit for their co-operation in this study and our colleagues for referring the patients; Dr. W. D. L. Fernando, forensic pathologist, for the necropsy reports; Professor Daphne Attygalle, for the histology; and Mr. Claude Perera, senior radiographer, for the illustrations.

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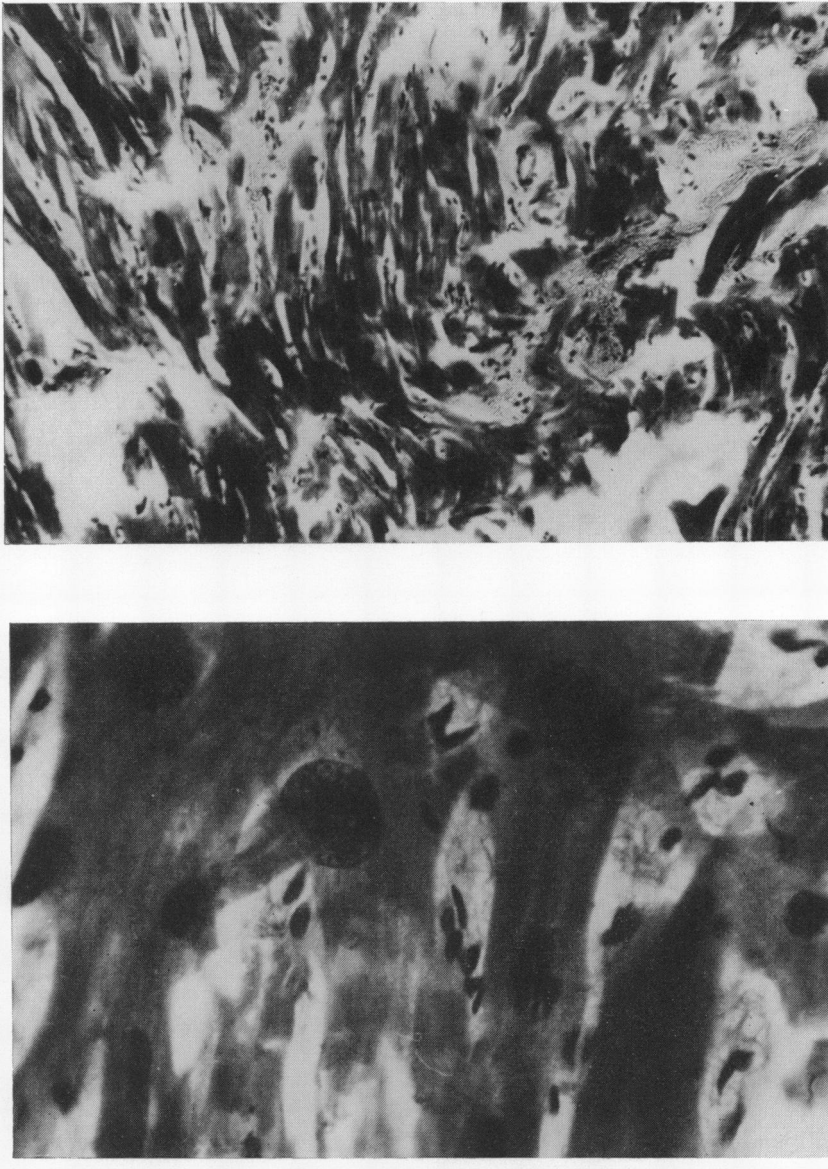


FIG. 7 and 8 *Medium and high power microscopical view of the heart in Fig. 6, showing gross hypertrophy of fibres, a mild degree of fibrosis, and some disorganization of muscle fibres. The hypertrophied muscle fibres have large bizarre nuclei.*

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